Effects of Age and Sleeping Position on Arousal from Sleep in Preterm Infants

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Study objectives: Preterm infants are at increased risk of sudden infant death syndrome (SIDS). We investigated whether the prone sleeping position impaired arousal from sleep in healthy preterm infants and whether this impairment was related to cardiorespiratory variables, temperature or postnatal age.

Design: Longitudinal

Setting/Participants: 14 healthy preterm infants (mean 32±0.4 weeks) were studied using daytime polysomnography on 4 occasions: 36-38 weeks postconception age, 2 to 3 weeks postterm, 2 to 3 months postterm, and 5 to 6 months postterm.

Interventions: N/A

Measurements: Multiple measurements of arousal threshold (cm H2O) in response to air-jet stimulation applied alternately to the nares were made in both active sleep and quiet sleep when infants slept both prone and supine.

INTRODUCTION

THE INCIDENCE OF THE SUDDEN INFANT DEATH SYNDROME (SIDS) HAS BEEN FOUND TO CONSISTENTLY HIGHER IN PRETERM AND LOW BIRTHWEIGHT INFANTS, and this incidence is inversely related to gestational age.1-4 It has been estimated that approximately 20% of all SIDS cases occur in the preterm population.4-6

The prone sleeping position has been identified as the major risk factor for SIDS in numerous studies carried out in many western countries.7-12 Various mechanisms have been proposed to explain the increased risk of prone sleeping, including rebreathing of expired gases13,14 overheating,15,16 and impairment of autonomic function.17,18 It has been postulated that arousal from sleep may be impaired in infants who die from SIDS.19 In a recent study, we demonstrated that in healthy term infants arousal responses are impaired in both quiet sleep (QS) and active sleep (AS) when infants slept both prone and supine.20 However, this relationship has not been investigated in a group that is at high risk for SIDS, such as preterm infants.

In this study we aimed to investigate whether arousal responses in healthy preterm infants were similarly affected by sleeping position. In addition, we wished to examine the effects of sleeping position on cardiorespiratory variables and body temperature and whether any effects were altered by postnatal age. Our study design also allowed us to determine whether the influence of sleeping position on arousal was age related, thereby providing a possible basis for explaining the increased risk for SIDS of the prone position compatible with the epidemiological evidence, which shows an increased risk between 2 and 4 months of age.

RESULTS

Arousal thresholds were significantly higher in both AS and QS when infants slept prone at 36 to 38 weeks postconception age and 2 to 3 months postterm but not at 2 to 3 weeks or 5 to 6 months postterm. These increases were independent of any sleep position-related changes in either rectal or abdominal skin temperature, respiratory rate, oxygen saturation or heart rate.

CONCLUSIONS: At the age when the risk of SIDS is highest, the prone position significantly impairs arousal from both active sleep and quiet sleep in healthy infants born prematurely. This impairment in arousability occurred with no clinically significant changes in cardiorespiratory parameters or body temperature. Decreased arousability from sleep in the prone position may explain its role as a risk factor for SIDS.

Key words: Arousal; prematurity; prone sleeping position; SIDS

Disclosures

This project was supported by SIDSaustralia, Sudden Infant Death Research Foundation of South Australia and SIDassist

Submitted for publication April 2002
Accepted for publication June 2002
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Recording Methods

Daytime polysomnography recordings were made from all infants between 10:00 AM and 4:00 PM. Electrodes for recording physiologic variables were attached to the baby while it fed, and when drowsy, the infant was placed in a bassinet under dim lighting and constant room temperature (22°-23°C). The study began once the infant had fallen
asleep. Infants were studied during both a morning and an afternoon sleep interrupted by a midday feed, when sleep position was changed from prone to supine or vice versa. The initial sleep position was randomized for the morning of the first study, and the opposite position used for the morning of the second study. All infants were routinely placed supine to sleep at home. When sleeping in the prone position, the infant’s head was turned to the side to avoid the face-straight-down position.

We made continuous recordings (Grass Polygraph Model 78A 16-channel recorder, Grass Instrument Company, Quincy MA) of electroencephalogram (EEG), electrooculogram (EOG), submental electromyogram (EMG), electrocardiogram (ECG), instantaneous heart rate, thoracic and abdominal breathing movements (Resp-ez Piezo-electric sensor, EPM Systems, Midlothian VA), expired CO2 (CO2/O2 Analyzer, Engstrom Eliza MC, Bromma, Sweden), blood oxygen saturation (SpO2) (Biox 3700e Pulse Oximeter, Ohmeda, Louisville CO), and abdominal skin and rectal temperature (YSI 400 series thermistor (NTC) probes).

Table 1—Number of infants studied and responses elicited to both test and sham stimuli at each study for each sleep state and sleep position

<table>
<thead>
<tr>
<th>37 WEEKS PCA</th>
<th>ACTIVE SLEEP</th>
<th>QUITE SLEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Infants</td>
<td>Prone</td>
<td>Supine</td>
</tr>
<tr>
<td>total stimulus presentations</td>
<td>436</td>
<td>355</td>
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<tr>
<td>total arousal thresholds</td>
<td>182</td>
<td>193</td>
</tr>
<tr>
<td>% arousal response</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>% spontaneous arousal</td>
<td>3</td>
<td>7</td>
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<table>
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<th>2-3 WEEKS PT</th>
<th>Number of Infants</th>
<th>total stimulus presentations</th>
<th>total arousal thresholds</th>
<th>% arousal response</th>
<th>% spontaneous arousal</th>
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<tbody>
<tr>
<td>Number of Infants</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>total stimulus presentations</td>
<td>397</td>
<td>302</td>
<td>465</td>
<td>319</td>
<td>169</td>
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<tr>
<td>total arousal thresholds</td>
<td>36</td>
<td>38</td>
<td>37</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>% arousal response</td>
<td>5</td>
<td>8</td>
<td>7</td>
<td>10</td>
<td>93</td>
</tr>
<tr>
<td>% spontaneous arousal</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
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<table>
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<th>5-6 MONTHS PT</th>
<th>Number of Infants</th>
<th>total stimulus presentations</th>
<th>total arousal thresholds</th>
<th>% arousal response</th>
<th>% spontaneous arousal</th>
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</thead>
<tbody>
<tr>
<td>Number of Infants</td>
<td>5</td>
<td>8</td>
<td>7</td>
<td>10</td>
<td>8</td>
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<tr>
<td>total stimulus presentations</td>
<td>93</td>
<td>89</td>
<td>142</td>
<td>164</td>
<td>42</td>
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<td>29</td>
<td>33</td>
<td>30</td>
<td>20</td>
<td>2</td>
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<tr>
<td>% arousal response</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
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Stimulus and Arousal Criteria

An established pulsatile air-jet technique (frequency 3 hertz for 5 seconds) delivered to the nostrils of the infant was used to induce arousal in both AS and QS, and arousal thresholds were calculated as described previously.21,22 Briefly, the stimulus was presented alternately to the left and right nostrils; if the infant failed to arouse, the air-jet pressure was increased when the stimulus was again presented to that nostril. Whenever an arousal response occurred, the pressure was then decreased. The change in driving pressure between each presentation was usually 100 centimeters of water, and the maximum driving pressure setting was 950 centimeters of water. Arousal threshold was calculated as the mean pressure between each arousal and nonarousal response. In the prone position in QS, stimuli at the maximum pressure sometimes failed to elicit an arousal. In these cases, an arousal threshold of 950 centimeters of water was recorded when two successive stimuli presented to the same nostril failed to elicit a response. In determining whether a presentation elicited an arousal response, a change in at least 3 of 4 criteria24 was required. The four criteria were a change in ventilation pattern of more than 2 breaths, an observed behavior response (usually a head movement away from the stimulus), a heart-rate acceleration of greater than 10% above baseline, and an increase in submental EMG activity. All of these changes must have occurred within 7 seconds of the stimulus onset, allowing for the time delay to reach peak heart-rate acceleration. For each physiologic variable, the 10 seconds of recording immediately preceding the stimulus presentation provided the baseline level used to assess the change in that variable.

DATA ANALYSIS

Data were first tested using the Kolmogorov-Smirnov normality test and the Levene median test for equal variance. Arousal thresholds for left and right nostrils were compared using a 1-way analysis of variance (ANOVA, SigmaStat v2, SPSS Inc, Chicago, IL). No difference between arousal thresholds was found between nostrils in either sleeping position; accordingly, data for each nostril have been pooled for all analyses of threshold. Mean arousal thresholds for AS and QS were calculated for each infant and compared between sleep positions within individual studies using a 2-way ANOVA for repeated measures. Missing values (3 for supine QS in study 1, 1 for prone AS in study 3, and 1 for prone AS in study 4) were estimated23 only when 1 of the 4 values was not obtained during a particular study. Arousal thresholds were compared across studies with 2-way ANOVA. The probability of spontaneous arousal was calculated as the number of spontaneous arousals occurring during each stimulus calibration (sham stimulus), expressed as a percentage of the total number of calibrations. Comparisons of spontaneous arousal probabilities between sleep states and sleeping positions were made using chi-square analysis. The lengths of sleep bouts were determined for complete bouts of both AS and QS, and those bouts terminating by arousals induced by our stimuli were excluded from analysis. Sleep-cycle length was determined as the time between the onset of successive bouts of AS, and only complete bouts of AS and QS were included in this analysis. Mean sleep bouts and sleep-cycle lengths were compared between studies using 2-way ANOVA. Physiologic variables were compared within studies with 2-way ANOVA for repeated measures. All values are expressed as mean ± SEM and a P value of less than .05 was considered significant.

RESULTS

A total of 1303 stimuli were presented at the 37 week PCA study, 1616 at the 2 to 3 week PT study, 1483 at the 2 to 3 months PT study, and 488 at the 5 to 6 months PT study. The total number of stimuli and responses elicited to both test and sham stimuli in each sleep state and sleep position are presented in Table 1.

Spontaneous Arousal

The probability of arousal in response to air-jet stimulation was significantly higher than the probability of spontaneous arousal from sleep in both sleep states and sleep positions in all studies (P<.001). The probability of spontaneous arousal from sleep was significantly higher in AS compared to QS at 2 to 3 months when infants slept supine (P<.01). The probability of spontaneous arousal was only affected by sleeping position in AS at 37 weeks when the probability was significantly higher in the supine position (P<.05). In supine QS, spontaneous arousals decreased with increasing postnatal age (P<.01).

Arousal Threshold

Effects of sleeping position. Arousal thresholds were elevated in the prone position in both AS and QS at 37 weeks PCA (P<.004; P<.05) and at 2 to 3 months PT (P<.05) (Figure 1a and 1b). At 2 to 3 weeks and 5 to 6 months PT, sleeping position had no effect on arousal in either sleep state.
Effects of sleep state. Arousal thresholds were elevated in QS compared to AS in both prone and supine positions at 2 to 3 weeks and 2 to 3 months but not at 37 weeks or at 5 to 6 months (Table 2).

Effects of postnatal age. Arousal thresholds in AS were not different across the ages studied in both sleeping positions. In QS when infants slept prone arousal thresholds were significantly higher at the 2 to 3 month study than at the 37 week study.

Physiologic Variables

To assess the possible effect of changes in physiologic variables, which could affect arousal threshold, we measured abdominal skin temperature, rectal temperature, heart rate, and oxygen saturation prior to each stimulus presentation. Mean respiratory rates were calculated over 3 minutes at the beginning of the first AS and first QS period for each sleep position during a time when there were no stimulus presentations. There was no difference in mean abdominal or rectal temperature, heart rate, respiratory rate, or oxygen saturation between sleeping positions in either AS or QS at any of the ages studied.

Sleep Characteristics

Durations of sleep bouts are presented in Table 3. There was no difference in the time spent in either sleep state between the two sleep positions at any of the four study ages. At 37 weeks PCA and 2 to 3 weeks PT, infants slept longer in AS than in QS in both the supine and prone positions. At 5 to 6 months PT, infants slept longer in QS than AS when sleeping supine.

DISCUSSION

This study has demonstrated that the prone position significantly impairs arousal from both AS and QS in healthy infants born prematurely at the age when SIDS incidence is highest (2-4 months). This impairment in arousability was independent of any significant changes in cardiorespiratory parameters or body temperature. Arousal from sleep is an important survival response to life-threatening events such as hypotension or prolonged apnea. By arousing from sleep, heart rate, blood pressure, and ventilation are increased and, importantly, a behavior response is evoked that allows body movement. Any impairment in arousability from sleep, such that ventilation or arterial pressure are not reestablished, could contribute to the final pathway to SIDS.

A consistent and unique feature of SIDS epidemiology is the age at which the incidence peaks, 2 to 4 months. The finding that sleeping position did not significantly affect arousability at 2 to 3 weeks or 5 to 6 months of age in either sleep state is in accordance with the epidemiologic data. This lack of effect was present despite the increase in arousal threshold with age in QS, which occurred in the prone position. Sleep position also impaired arousability at the preterm study between 36 and 38 weeks of PCA. This age period has not been reported to be a high-risk period for SIDS, as the universally accepted definition for SIDS is the death of an infant between 1 month and 1 year of age. Our finding highlights the importance of placing prematurely born infants to sleep in the supine position as soon as medically appropriate.

We have previously demonstrated that sleeping position has a marked influence on arousal from sleep in healthy term infants, with arousal being depressed in the prone position. This impairment in arousability was also independent of any significant changes in cardiorespiratory parameters or body temperature. Caution must be taken in comparing the results obtained in preterm infants in this study directly with those of term infants studied in an identical protocol, as mean age at the 2 to 3 month and 5- to 6-month studies were different (P<.02). Mean age for term infants at the 2 to 3 month study was 74±1 days and at the 5 to 6 month study was 182±4 days. However, at 2 to 3 weeks, when ages were comparable, there was no difference in arousal threshold in either position in either Q5 or AS. Similarly, at 2 to 3 months, when there was only a 5-day difference in ages between the term and preterm groups, there was also no difference in arousability in either sleep position or sleep state. At 5 to 6 months of age, the supine position was more arousable in Qs when sleeping in the supine position (P<.05); however, ages differed by 13 days between the groups. It thus appears that the effects of sleep position on arousal from sleep are similar in healthy term and preterm infants.

A number of reasons have been suggested as to why the prone position may present an increased risk of SIDS. These include reduced inspired oxygen or increased carbon dioxide levels due to rebreathing and increased body temperature due to reduction in heat loss from the face and head. All of our infants were placed prone with their face to the side, and efforts were made to turn the head if infants attempted to bury their faces in the bedding. Impairment in arousal occurred with no physiologically significant change in either rectal or abdominal skin temperature, oxygen saturation, or respiratory rate. Other studies have suggested that autonomic function is impaired in the prone position, as heart rate is elevated and variability is decreased. Although we did not examine heart-rate variability in our study, heart rate was not significantly elevated in the prone position in either sleep state at any of the ages studied.

Sleep-state exerts a marked influence on arousal from sleep in term infants between 2 to 3 weeks and 5 to 6 months of age. Our findings from this study are consistent with those previously published by our group in healthy preterm infants sleeping supine, that in this sleep-state–related difference is not apparent in infants before term. In this earlier study, arousal thresholds were also not different between sleep states at 2 to 3 weeks of age. The findings of this current study—that arousal thresholds are elevated in QS compared with AS at both 2 to 3 weeks and 2 to 3 months of age—may be explained by the fact that the infants were slightly older than those previously studied (mean 7.5±2 days, range 2-21 days) and, thus, are not directly comparable. However, this finding supports our contention that sleep-state differences in arousability are affected by infant maturation.

Other workers have reported that the prone sleeping position increased the time spent in Q5 and we have previously demonstrated that arousal thresholds increased with the amount of time spent asleep in term infants at 2 to 3 months. However, in this study we demonstrated no difference between bout lengths in the two sleeping positions at any of the ages studied and so this could not explain our findings.
It has previously been reported that spontaneous arousals from sleep are less frequent when infants sleep prone. In this study this was only apparent in AS at 37 weeks. This may have been because our measurement of probability of spontaneous arousal was confined to the period of stimulus calibration (7 seconds) immediately prior to each stimulus presentation. The total number of spontaneous arousals from sleep could not be determined in this study design because we were repeatedly evoking arousals with our air-jet stimulus.

The possibility that preterm infants exhibit a delay in maturation may also be reflected in the finding that preterm infants die of SIDS at a later postnatal age, but a younger PCA, than do term infants. Malloy and Hoffman demonstrated that premature infants born at 29 to 32 weeks postconception age impairs arousal in both term and preterm infants at this age may be important in understanding the mechanisms involved in SIDS.

ACKNOWLEDGMENTS

The authors thank the staff of Newborn Services and Jessie McPherson Private Hospital at the Monash Medical Centre and the parents and infants who participated in this study. We also wish to thank Professor Richard Harding, Department of Physiology, Monash University, for his interest in this project.

REFERENCES


